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EXAMINER	
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ART UNIT	PAPER NUMBER
1641	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/606,301	DIESSEL ET AL.	
	Examiner	Art Unit	
	Leon Y Lum	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-76* is/are pending in the application.

4a) Of the above claim(s) *31-76* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 June 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *20041210*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 1-30 in the reply filed on 24 November 2004 is acknowledged. The traversal is on the ground(s) that both groups I and II can be examined without serious burden. This is not found persuasive because Group II requires a search for devices that measure the current or voltage between a first counterelectrode and measurement electrode, which is not a search that is required for Group I. Group I requires a search for method steps of bringing at least one analyte label with an electrically active labeling unit into contact with the biofunctional surface before the analyte is contacted with the biofunctional surface, which is a search that is not required for Group II.

The requirement is still deemed proper and is therefore made FINAL.

Information Disclosure Statement

2. The information disclosure statement filed 25 June 2003 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because foreign patent documents DE 43 18 519 A1 and DE 198 60 547 C1 do not have English translations, except for the abstracts. The documents have been placed in the application file, but only the abstracts referred to therein have been considered

as to the merits. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609 ¶ C(1).

Specification

3. The abstract of the disclosure is objected to because lines 11-12 of the abstract are not directed towards the invention and contain a reference to section 1.72(b) of the Code of Federal Regulations. Correction is required. See MPEP § 608.01(b).

4. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required:

Page 3, line 22 to page 4, line 9 in the specification recites DC measurements. However, there is no recitation anywhere in the specification of a DC voltage superimposed on the time-varying voltage, as is claimed in the instant claims.

Claim Objections

5. Claims 4 and 8 are objected to under 37 CFR 1.75 as being a substantial duplicate of claims 3 and 7, respectively. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8. In claim 1, line 6, the phrase "the analyte" is vague and indefinite. The instant claim recites that there can be more than one analyte with the phrase "at least one analyte" in line 1. In the event that there is more than one analyte, it is unclear which analyte the instant phrase refers to.

9. In claim 1, line 21, the phrase "a second or subsequent counterelectrode" is vague and confusing. The instant claim recites that there can be "one or more counterelectrodes" in line 7. In the event that there is only one counterelectrode, it is confusing as to how a second or subsequent counterelectrode can be present, as claimed by the instant phrase.

10. In claim 6, lines 3-4, the phrase "the use of suitable equivalent circuit diagrams" is vague and indefinite. The specification does not define the phrase and it is unclear how suitable equivalent circuit diagrams are used.

11. In claim 12, line 1, the phrase "an analyte molecule" is vague and indefinite. It is unclear whether the instant phrase is directed towards the at least one analyte in line 1 of the instant claim, or to another analyte not previously mentioned.

12. In claim 18, line 2, the term "and/or" is vague and indefinite. It is unclear whether the limitations following the instant term are included with the limitations preceding the term.

13. Claim 1 recites the limitations "a first counterelectrode" and "the first counterelectrode" in lines 16 and 18, respectively. There is insufficient antecedent basis for these limitations in the claim. The instant claim recites "one

or more counterelectrodes" in line 7, but does not recite a "first counterelectrode" prior to the instant limitation.

14. Claim 5 recites the limitation "the impedance" in line 1. There is insufficient antecedent basis for this limitation in the claim.

15. Claims 5-6 recite the limitation "the first or another counterelectrode" in line 2 of the claims. There is insufficient antecedent basis for this limitation in the claim. The instant claim recites "one or more counterelectrodes" in line 7. If there is only one counterelectrode, there is no antecedent basis for another counterelectrode as claimed by the instant limitation.

16. Claim 11 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: how the unlabeled analyte in line 3 contributes to the method of detecting the "at least one analyte" (line 1). In addition, it is unclear as to which analyte is being detected: the labeled analyte or unlabeled analyte.

17. Claim 27 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: The specification recites the step of HRP induced polymerization of monomers of

electrically conductive polymers on page 8, lines 7-9. However, the specification does not disclose how the polymerization of monomers results in the detecting at least one analyte using a recognition reaction, as recited in lines 1-2 of claim 1. One of ordinary skill in the art at the time of the invention would not know how to obtain detection of the at least one analyte from the steps recited in the instant claim since essential steps linking the polymerization and detecting steps are missing.

Claim Rejections - 35 USC § 102

18. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

19. Claims 1, 3-8, 9-10 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Choong et al (WO 01/42508 A2).

In the instant claims, Choong et al reference teaches a method for detecting at least one analyte using a recognition reaction, said method comprising providing a device comprising a measurement electrode with a biofunctional surface, the biofunctional surface having recognition elements for the analyte, one or more counterelectrodes, and a liquid electrolyte between the

measurement electrode and the one or more counterelectrodes, bringing at least one analyte labeled with an electrically active labeling unit into contact with the biofunctional surface, the electrically active labeling unit having been bound to the analyte before the analyte is contacted with the biofunctional surface, applying a time-varying voltage between a first counterelectode and the measurement electrode, and measuring the current between the first counterelectrode and the measurement electrode, by disclosing an array of microelectrodes in contact with a supporting substrate to which probes are immobilized, at least one counter-electrode in electrochemical contact with the supporting substrate, and an electrolyte solution in contact with the plurality of microelectrodes (page 6, lines 27-32), wherein during electrochemical detection of nucleic acid hybridization, a probe bound to a microelectrode hybridizes with an electrochemically-labeled target molecule (page 47, lines 24-25), and wherein electric and electrochemical methods can be used to detect molecular interactions between probe molecules and electrochemically-labeled target molecules, including measuring electric current as a function of voltage, wherein the voltage applied is AC (page 11, lines 14-22 and page 32, lines 30-36). Although Choong et al reference does not explicitly disclose that the electrochemical label is bound to the target molecule before the molecule hybridizes with the probe, since the reference teaches that the probe is hybridizes to an "electrochemically-labeled target molecule", it is recognized that the target molecule has already been bound to the label prior to coming into contact with the probe.

With regards to claims 3-4, Choong et al reference teaches that the time-varying voltage is an alternating current, by disclosing the AC voltage, as stated above (page 11, lines 14-22 and page 32, lines 30-36).

With regards to claim 5, Choong et al reference teaches that the impedance between the measurement electrode and the first counterelectrode is determined, by disclosing the step of detecting changes in AC impedance (page 32, lines 10-11).

With regards to claim 6, Choong et al reference teaches that capacitance between the measurement electrode and the first counterelectrode is derived from the impedance measurement with the use of suitable equivalent circuit diagrams, by disclosing semicircular curves that can be used to obtain double layer capacitance by equivalent circuit simulation (page 42, lines 8-17; and Figures 3A-B).

With regards to claims 7-8, Choong et al reference teaches that the DC voltage is superimposed on the time-varying voltage, by disclosing that DC potentials and AC voltamettry can be applied with combinations thereof (page 32, lines 24 and 30-36). Since combinations of alternating and direct currents can be applied, one example of a combination would be DC voltage superimposed on AC voltage.

With regards to claims 9-10, Choong et al reference teaches that the recognition reaction constitutes a DNA or SNP assay, by disclosing that target nucleic acids can be DNA (page 15, lines 12-30) and that single polymorphisms can be detected (page 33, lines 1-2).

Claim Rejections - 35 USC § 103

20. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

21. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

22. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of

35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

23. Claim 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over Choong et al (WO 01/42508 A2) in view of Butler (US 4,006,059).

Choong et al reference has been disclosed above and additionally teaches that the microelectrodes are covered with a layer of polymeric hydrogel wherein protein probes are attached to the hydrogel (page 8, line 29 to page 9, line 4), but fails to teach that the recognition elements are non-covalently immobilized on the measurement electrode.

Butler reference discloses immobilization of proteins to gels by adsorption, in order to provide a much more convenient and inexpensive method to immobilize proteins since no covalent chemical bond is formed (column 1, lines 34-42).

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Choong et al with immobilization of proteins to gels by adsorption, as taught by Butler, in order to provide a much more convenient and inexpensive method to immobilize proteins since no covalent chemical bond is formed. One of ordinary skill in the art at the time of the invention would have reasonable expectation of success in non-covalently immobilizing proteins to a substrate, as taught by Butler, in the method of Choong et al, since Choong et al teach the attachment of proteins to a hydrogel, and the adsorption of proteins taught by Butler is also on gels.

24. Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Choong et al (WO 01/42508 A2) in view of Giegel et al (US 4,517,288).

Choong et al reference has been disclosed above, but fails to teach that an unlabeled analyte is also brought into contact with the biofunctional surface.

Giegel et al reference teaches the step of labeled and unlabeled analyte compounds competing for binding sites on a binding material, in order to perform an immunochemical assay (column 1, lines 49-55).

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Choong et al with step of labeled and unlabeled analyte compounds competing for binding sites on a binding material, as taught by Giegel et al, in order to perform an immunochemical assay. One of ordinary skill in the art at the time of the invention would have reasonable expectation of success in including a competitive assay, as taught by Giegel et al, in the method of Choong et al, since Choong et al teach that probes can be antibodies and (page 9, lines 2-4) target analytes can be immunoglobulins (page 16, lines 16-18).

25. Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Choong et al (WO 01/42508 A2) in view of Bahl et al (US 5,324,829).

Choong et al reference has been disclosed above, but fails to teach that an analyte molecule is labeled with a plurality of electrically active labeling units.

Bahl et al reference discloses multiple labels for defined places in a target sequence, in order to provide more user control with nucleotide sequence probes, which comprise signal generating moieties that include detectable labels, wherein the nucleotide sequences vary widely in their specific sequences (column 3, line 65 to column 4, line 23).

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Choong et al with multiple labels for defined places in a target sequence, as taught by Bahl et al, in order to provide more user control with nucleotide sequence probes, which comprise signal generating moieties that include detectable labels, wherein the nucleotide sequences vary widely in their specific sequences. One of ordinary skill in the art at the time of the invention would have reasonable expectation of success in including multiple labels to bind a target, as taught by Bahl et al, in the method of Choong et al, since both Choong et al and Bahl et al references teach binding of probes to DNA targets.

26. Claims 13-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Choong et al (WO 01/42508 A2) in view of Ewart et al (US 5,922,537).

Choong et al reference has been disclosed above, but fails to teach that the electrically active labeling unit has a dielectric constant in the range of from 5 to 15,000(claim 13) or in the range of between 10 and 1,500 (claim 14).

Ewart et al reference teaches nanoparticles having a dielectric constant as close as possible to 1 (column 14, lines 19-20), wherein the properties of the

particle can be selected to enhance its dielectric properties (column 5, lines 2-6), and wherein the dielectric label/tag is selected to contribute the dominant dielectric constant in the complex (analyte-recognition molecule-dielectric label/tag), in order to minimize analyte-to-analyte and assay-to-assay variation which is inherent in the analyte-recognition complexes themselves (column 14, lines 19-38).

It would have been obvious at the time of the invention to modify the method of Choong et al with nanoparticles having a dielectric constant as close as possible to 1, wherein the dielectric label/tag is selected to contribute the dominant dielectric constant in the complex (analyte-recognition molecule-dielectric label/tag), as taught by Ewart et al, in order to minimize analyte-to-analyte and assay-to-assay variation which is inherent in the analyte-recognition complexes themselves. One of ordinary skill in the art at the time of the invention would have reasonable expectation of success in including a nanoparticle with a specific dielectric, as taught by Ewart et al, in the method of Choong et al, since Choong et al teach hybridization assays, and the nanoparticles taught by Ewart et al can also be used in hybridization assays (column 3, line 17).

Ewart et al reference discloses the claimed invention except for a dielectric constant in the range of from 5 to 15,000 or in the range of between 10 and 1,500. It would have been obvious to one having ordinary skill in the art at the time the invention was made to select nanoparticles that have dielectric constants in the range of from 5 to 15,000 or in the range of between 10 and 1,500, since it has been held that where the general conditions of a claim are

disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 105 USPQ 233. Since Ewart et al reference discloses that properties of the dielectric label/tag can be selected, as stated above, the dielectric constant corresponding to the selected label/tag can also be selected.

27. Claims 15-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Choong et al (WO 01/42508 A2) in view of Kausch et al (US 5,665,582).

Choong et al reference has been disclosed above, but fails to teach that the electrically active labeling unit has a size in the range of from 1 to 2 nm.

Kausch et al reference teaches magnetic particles as labels of the order of 1nm, in order to label small biological materials (column 11, line 65 to column 12, line 6).

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Choong et al with magnetic particles as labels of the order of 1 nm, as taught by Kausch et al, in order to label small biological materials. One of ordinary skill in the art at the time of the invention would have reasonable expectation of success in including labels on the order of 1 nm, as taught by Kausch et al, in the method of Choong et al, since both Choong et al and Kausch et al teach the labeling of small biological materials.

In addition, it would have been obvious to one having ordinary skill in the art at the time the invention was made to select an electrically active labeling unit has a size in the range of from 1 to 2 nm, since it has been held that where the

general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 105 USPQ 233.

28. Claims 18-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Choong et al (WO 01/42508 A2) in view of Weiss (US 5,858,666).

Choong et al reference has been disclosed above, but fail to teach that the electrically active labeling unit is an Au complex.

Weiss reference teaches that target label may be a gold colloid, in order to provide a label that will cause a strong response irrespective of the frequency of AC signal, thereby causing tuning to be less of an issue (column 7, line 54 to column 8, line 6).

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Choong et al with a target label that may be a gold colloid, as taught by Weiss, in order to provide a label that will cause a strong response irrespective of the frequency of AC signal, thereby causing tuning to be less of an issue. One of ordinary skill in the art at the time of the invention would have reasonable expectation of success in labeling targets with gold colloid, as taught by Weiss, in the method of Choong et al, since Choong et al teach assays using labeled analytes with applied AC detection methods, and the labeled target of Weiss is able to give a response in the presence of an AC signal.

29. Claim 20 is rejected under 35 U.S.C. 103(a) as being unpatentable over Choong et al (WO 01/42508 A2) in view of Weiss (US 5,858,666) as applied to claims 1 and 18-19 above, and further in view of Buechler (US 5,885,527).

Choong et al and Weiss references have been disclosed above, but fail to teach nanoparticles that are made of titanates.

Buechler reference teaches titania nanoparticles in order to provide particles with a surface area that allows greater protein coating than larger latex particles (column 12, line 63 to column 13, line 6).

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Choong et al and Weiss with titania nanoparticles, as taught by Buechler, in order to provide particles with a surface area that allows greater protein coating than larger latex particles. One of ordinary skill in the art at the time of the invention would have reasonable expectation of success in applying titania nanoparticles, as taught by Buechler, to the method of Choong et al and Weiss, since Choong et al teach that labels can bind to protein analytes (page 16, lines 8-10), and the titania nanoparticle taught by Buechler can also bind to proteins.

30. Claims 21-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Choong et al (WO 01/42508 A2) in view of Weiss (US 5,858,666) as applied to claims 1 and 18-19 above, and further in view of Tarcha et al (US 5,252,459).

Choong et al and Weiss references have been disclosed above, but fail to teach that the electrically active labeling units nonconductive particles with a metallic coating (claim 21) or polythiophenes (claims 22-23).

Tarcha et al reference teaches a nonmetallic substance coated with metal, in order to produce a signal that is visually detectable and measurable by an instrument (column 1, lines 56-65), and also teaches organic polymer latex particles including poly(thiophene) (column 2, lines 20-39) as indicator reagents that label a specific binding member and can include copolymers (column 10, lines 59-64), in order to provide a colored polymer particle that overcome the limited color intensity of metallic particles (column 1, line 66 to column 2, line 4; and column 2, lines 57-62), wherein a specific binding member can be DNA (column 3, lines 5-14).

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Choong et al and Weiss with coated with metal, in order to produce a signal that is visually detectable and measurable by an instrument, and organic polymer latex particles including poly(thiophene) as indicator reagents that label a specific binding member and can include copolymers, as taught by Tarcha et al, in order to provide a colored polymer particle that overcome the limited color intensity of metallic particles. One of ordinary skill in the art at the time of the invention would have reasonable expectation of success in attaching poly(thiophene) latex particles to specific binding members, as taught by Tarcha et al, in the method of Choong et al and

Weiss, since Choong et al and Weiss teach the labeling of DNA analytes, and the poly(thiophene) latex particles taught by Tarcha et al can also bind to DNA.

31. Claim 24 is rejected under 35 U.S.C. 103(a) as being unpatentable over Choong et al (WO 01/42508 A2) in view of Weiss (US 5,858,666) as applied to claims 1 and 18-19 above, and further in view of Tarcha et al (US 5,252,459) as applied to claims 22-23 above, and further in view of Babinec et al (US 6,203,727 B1).

Choong et al, Weiss, and Tarcha et al references have been disclosed above, but fail to teach that the conductive polymer is polyethylene dioxythiophene.

Babinec et al reference teaches polyethylene dioxythiophene, in order to provide an intrinsically-conductive polymer that possess excellent conductivity, thermal stability, and can be desirable in electroactive applications such as sensors (column 1, line 63 to column 2, line 9; and column 2, lines 37-60).

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Choong et al, Weiss, and Tarcha et al with polyethylene dioxythiophene, as taught by Babinec et al, in order to provide an intrinsically-conductive polymer that possess excellent conductivity, thermal stability, and can be desirable in electroactive applications such as sensors. One of ordinary skill in the art at the time of the invention would have reasonable expectation of success in applying polyethylene dioxythiophene as a conducting polymer, as taught by Babinec et al, in the method of Choong et al, Weiss, and

Tarcha et al, since Tarcha et al teach that polythiophenes can be used to label targets, and polyethylene dioxythiophene is one example of a polythiophene.

32. Claims 25-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Choong et al (WO 01/42508 A2) in view of Farmakovski et al (WO 00/11473).

Choong et al reference has been disclosed above, but fails to teach that the labeling unit is one of enzymes which form electrically active labeling units by the reaction of a substrate (claim 25), wherein the labeling unit comprises horseradish peroxidase (HRP) (claim 26).

Farmakovski et al reference teaches a horseradish peroxidase enzyme conjugated to a competing receptor that is capable of converting a substrate which directly affects the redox composition of the electroconductive polymer coating of the sensing electrode into a product which has not detectable effect on the redox composition of the electroconductive polymer (page 21, lines 14-22), wherein the enzyme conjugated to secondary receptors that bind to an analyte after the analyte is immobilized on electrode-bound receptors (page 19, line 33 to page 20, line 24), in order to present an alternative to the use of a charge label and to transducer a chemical signal associated with the concentration of the analyte into a measureable electrical signal (page 19, lines 25-32).

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Choong et al with a horseradish peroxidase enzyme conjugated to a competing receptor that is capable of converting a

substrate which directly affects the redox composition of the electroconductive polymer coating of the sensing electrode into a product which has not detectable effect on the redox composition of the electroconductive polymer, wherein the enzyme conjugated to secondary receptors that bind to an analyte after the analyte is immobilized on electrode-bound receptors, as taught by Farmakovski et a, in order to present an alternative to the use of a charge label and to transducer a chemical signal associated with the concentration of the analyte into a measureable electrical signal. One of ordinary skill in the art at the time of the invention would have reasonable expectation of success in using horseradish peroxidase enzyme as an analyte label, as taught by Farmokovski et al, in the method of Choong et al, since Choong et al teach electrical detection using labeled analytes, wherein the analytes are cardioactive drugs such as digoxin (page 16, line 22), and the electrical detection of labeled analyte taught by Farmovski et al also includes digoxin analytes (page 17, line 31).

33. Claims 27-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Choong et al (WO 01/42508 A2) in view of Farmakovski et al (WO 00/11473) as applied to claims 1 and 25-26 above, and further in view of Zemel et al (US 5,420,237).

34. Choong et al and Farmakovski et al references have been disclosed above, but fail to teach that the step of converting a substrate is polymerization of a conductive polymer (claim 27), wherein the conductive polymer is polyaniline (claim 28).

Zemel et al reference teaches the enzymatic synthesis of electrically conductive polyanilines, in order to form a conducting film (column 1, lines 9-16), wherein the enzyme is horseradish peroxidase (column 6, lines 3-5).

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Choong et al and Farmakovski et al with the enzymatic synthesis of electrically conductive polyanilines, as taught by Zemel et al, in order to form a conducting film. One of ordinary skill in the art at the time of the invention would have reasonable expectation of success in polymerizing polyanilines, as taught by Zemel et al, in the method of Choong et al and Farmakovski et al, since Farmakovski et al teach coating electrodes with polyaniline by electrochemical synthesis from a monomer solution to form an electrically conductive electrode (page 10, line 24 to page 11, line 2), and the step of Zemel et al is one example of a method to perform polymerization of polyaniline to form a conducting film.

35. Claims 29-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Choong et al (WO 01/42508 A2) in view of Farmakovski et al (WO 00/11473) as applied to claims 1 and 25-26 above, and further in view of Zemel et al (US 5,420,237) as applied to claim 27 above, and further in view of Hackett et al (US 5,759,774).

Choong et al, Farmakovski et al, and Zemel references have been disclosed above, but fail to teach that the electrically active labeling units are autometallographically enlarged using Au.

Hackett et al reference teaches antibody-enzyme conjugates comprising enzyme-metals such as colloid gold, in order to amplify the sensitivity of assay detection (column 16, lines 17-45).

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Choong et al, Farmakovski et al, and Zemel with antibody-enzyme conjugates comprising enzyme-metals such as colloid gold, as taught by Hackett et al, in order to amplify the sensitivity of assay detection. One of ordinary skill in the art at the time of the invention would have reasonable expectation of success in including enzyme-metal conjugates that include colloid gold, as taught by Hackett et al, in the method of Choong et al and Farmakovski et al, since Farmakovski et al teach that the HRP enzyme can be bound to antibody receptors (page 15, lines 8-17), and the enzyme-metal conjugate that includes colloid gold, as taught by Hackett et al, can also bind to antibodies.

Conclusion

36. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leon Y Lum whose telephone number is (571) 272-2878. The examiner can normally be reached on 8:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax

phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

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